system, the software calculates 5 million GSA steps in under 6 hours using 4 processors in one node.
Predicted structures can be refined with molecular dynamics simulations and used to study proteins whose conformation can not be determined with experimental methods. These structures can be used in protein engineering, drug development and biotechnological research.

1173-Pos Board B65
Novel Physics-Based Protein Structure Refinement Method
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Refinement of low-resolution protein structures is still a major problem despite the advancements in structure prediction and refinement methods. We have recently developed a new approach, which mimics the mechanism of chaperones that rehabilitate misfolded proteins by causing them to unfold, and then giving them a new chance to refold. The target protein is unfolded by selectively pulling different ends, using geometric based simulation techniques, FRODA (1), and then refolded by the zipping and assembly method (ZAM) (2-3). During these steps, the unfolded trajectories are used to identify conserved backbone dihedral angles and hydrophobic-hydrophobic contacts, and then this acquired information is used as energetic restraints to enforce contacts and dihedral angles during refolding, through 10ns of replica-exchange molecular dynamics using the AMBER force field with implicit solvation. We have tested this refinement method on CASP9 and CASP10 targets, and observed that usually misfolded parts of the chain unfold first and most importantly refolds to produce a better refined structure.
1. de Graff, Adam M.R.; Shannon, Gareth; Farrell Daniel W.; Williams, Philip M.; Thorpe, M.F. Biophys J. (2011) 101(3):736-744
2. Ozkan, SB; Wu, GA; Chodera, JD; Dill, KA Proc. Natl Acad. Sci USA (2007) 104:11987-11992.
3. Glembo, TJ and Ozkan SB, Biophys. J. (2011) 98:1046-1054

1174-Pos Board B66
New Methods to Improve Protein Structure Prediction and Refinement
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We have developed and combined several novel methods to improve protein structure prediction from the amino acid sequence, and the structural refinement of protein models. One of the most promising developments in protein structure prediction are many-body potentials that take into account dense packing, and cooperativity of interactions in protein cores. We developed a method that uses whole protein information filtered through machine learners to score protein models based on their likeness to native structures. Testing on CASP 9 targets showed that our method is superior to the common DFIRE and its derivatives as well as to the current version of RWPlus, both of which are considered a standard in the field. By combing statistical contact potentials with entropies from the elastic network models of proteins we can compute free energy and improve coarse-grained modeling of protein structure and dynamics. The consideration of protein flexibility and its fluctuational dynamics improves protein structure prediction, and leads to a better refinement of computational models of proteins. We proposed a novel protein structural refinement procedure based on Anisotropic Network Model (ANM) of protein fluctuational dynamics and Go-like model of energy score. The starting structures were models from past CASP experiments. We changed positions of C-alpha atoms using ANM, creating a new set of 250 structures from the initial model, and computed energies of these structures using Go-like energy score. The top 5 coarse-grained structures were fully rebuilt with BBQ and Scrwl4. To remove bond stretches and the excluded volume clashes, short Molecular Mechanics simulations (up to 10,000 steps) were performed with OPLS-AA force field and implicit solvent GBSA-OBC. The whole structural refinement process was performed iteratively leading to the improvement of average RMSD from 3.8A to 2.6A in 50 iterations.

1175-Pos Board B67
Absolute Quality Assessment of Protein Models
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Modeling methods increasingly attempt to close the gap between the number of known protein-coding sequences to that of structurally resolved proteins, but the results of these methods have been of mixed success. Adequate models can be built for proteins with high sequence similarity to a structurally resolved protein and occasionally modeling even succeeds in the absence of a good template, but currently no method exists to reliably rate the quality of the models. Many protein structure prediction methods rate protein models using an established scoring function by comparing the energies of an ensemble of structures and choosing the lowest energy members of said ensemble as the prediction. The acceptance of theoretical protein models is limited in the life-sciences, as currently no method exists to rate the quality of a protein model a-priori, i.e. from the model alone.
Here we investigate an approach to provide an a-priori estimator of the quality of a protein model using a free-energy scoring function[1], without comparing it to a competing ensemble. We devised a N-dimensional statistical test based on the per-residue energies of amino acids in a set of high-resolution experimental structures. The quality of the protein structures can be assessed by comparison against these statistics. We were able to discriminate the low quality models for 93% of the 160 proteins tested, which is increased further to 99%, when excluding proteins, which bind cofactors or DNA; interactions not considered by the energy model or the training set. In combination with bioinformatics based methods that exclude proteins that are not covered by the scoring function, this measure for quality assessment of protein models may help increase the acceptance of qualified theoretical protein models in the life-sciences.
[1] Verma, A.,Wenzel, W. (2009). A Free-Energy Approach for All-Atom Protein Simulation. Biophys.J 96,3483-3494.

1176-Pos Board B68
MQAPmulti2 and MQAPsingle2:Toward the Estimation of Model Quality When Not Only Many Models are Available
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We propose two new methods for the estimation of the quality of protein models. MQAPmulti2 performs well when scoring hundreds of alternative models, but also it can be applied when only a few models (~20) are available. We optimized MQAPmulti (developed earlier by Pawlowski and Bujnicki) to perform better when less than hundreds models are available.
The MQAPmulti2 prediction is based on three components: 1) TrueMQAP_component - scoring is based on statistical and agreement potentials; 2) CLUST_component, which clusters models on the base of GDT_TS and SQ_score (our modification of Q-score that works by estimating the structural relatedness between two protein structures based on comparison of intramolecular distances); 3) CORR_component, a correlation based method that combines predictions of the TrueMQAP_componet with pair-wise models comparisons measured by GDT_TS and SQ_score. Finally, all of these components are used to predict the global quality of a model. To do so, on the base of the number of input models, the program chooses one of 3 regression models that describe the relationship between initial parameters and the global quality. These three regression models were created for following numbers of input models: 20, 150, 300 or more.
MQAPsingle2, that is a variant of the MQAPmulti2 program, that operates as a quasi-single model MQAP. This method applies MQAPmulti2 algorithm, however a model to be scored is not compared to the input models, but to models generated by GeneSilico fold prediction metaserver.
MQAPmulti2 was trained and tested for *CASP7th, 8th and 9th* models dataset by using 10-fold cross validation procedure. The value of Pearson's correlation coefficient between MQAPmulti2 global score and the GDT_TS is 0.712, 0.819 and 0.917 for cases of 20, 150 and 300 or more available input models, respectively.

1177-Pos Board B69
Modeling Temperature-Dependent Ion Channel Protein Structural Changes with Rosetta
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Temperature-sensing ion channels are thought to adopt different conformations at varying temperatures, driven by a significant difference in free energy between the closed and open states. In support of this notion, we previously observed with site-directed fluorescence recordings that pore region undergoes substantial structural rearrangements during the heat activation of TRPV1 channels. Temperature-driven structural changes have also been suggested in other protein regions and channel types. To reveal such structural changes, we are exploring the Rosetta modeling method to predict channel protein structural differences at two different temperatures.